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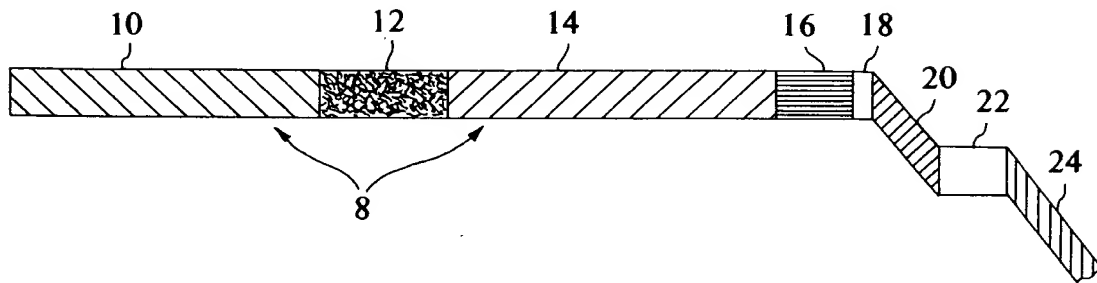
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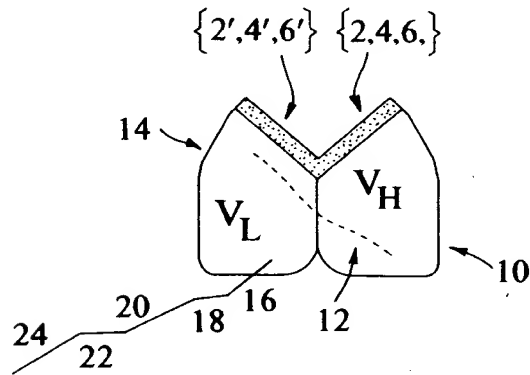
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SINGLE CHAIN BINDING POLYPEPTIDE



Extended Polypeptide

FIG. 1(a)



Folded Protein

FIG. 1(b)

2050E0 12/88350

SINGLE CHAIN
BINDING POLYPEPTIDE SHOWING
LOCATIONS OF COMPLEMENTARITY
DETERMINING REGIONS, POLYPEPTIDE
SPACER REGIONS, AND EFFECTOR REGIONS

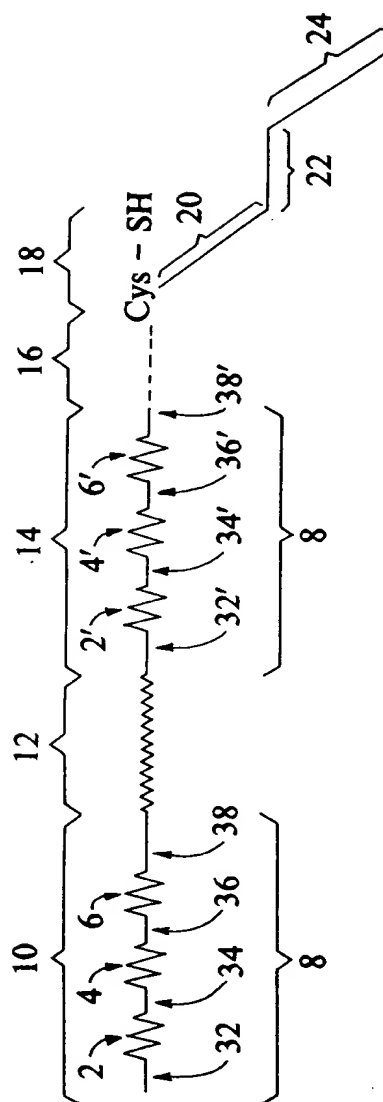


FIG. 2

C6.5 sFv
AMINO ACID SEQUENCE

(N-terminus to C-terminus)

-QVQLQSGAELKPGESLKISCKGSGYSTSYWIAWRQMPGKLEYMGL
IYPGDSDTKYSFQGVTTISVDKSVSTAYLQWSSLKPSDSAIFYCARHD
VGYCSSNCAKWPEYFQHWGQGLTVTVSSGGGGGGGGSG
GGGSQSVLTQPPSVSAAPGQKVTISCSGSSNIGNNYVSWYQLPGTAPK
LLIYHTNRPAGVPDRFSGSKSGTSASLAISGRSEDEADYYCAAWDDSL
SGWVFGGGLTLTVLG

FIG. 3

C6.5 sFv
NUCLEOTIDE SEQUENCE

5'caggtgcagctgttgcagctctggggcagagttgaaaaaacccggggagtgcttgaagatctcttgaaggttctggataca
gcttaccagctactggatcgccctgggtgcgccagatgccccgggaaaggcctggaggtacatggggctcatctatcctggtgactc
tgacaccaaatacagcccgctccttccaaaggccagggtcaccatctcagtcagacagtcgcagcactgcctacttgcaatggagc
agtcctgaagccctcggacagcgccgtgtattttgtgcgagacatgacgtgggatatgtgcagtagttccaaactgogcaaatggcc
tgaatacttccagcattggggccaggcgaccctgggtaccgtctctcctcaggtggagggcgggttcagggcgagggtgctctggcg
gtggcggatcgagctgtgttgacgcagcgccctcagtggtctggccccccagggacagaaaggtcaccatctcctctctggaa
gcagctcccaacattgggaataattatgtatcctgtaccagcagctccacaggaaacagcccccaactcctcatctatggtcacacca
atggccccgcagggtccctgaccgattctctgtggtcccaagcttggcacctcagcctccctggccatcagtggggttcgggtccga
ggataggctgattactgtgcagcatgggatgacagcctgagtgggtgggtgttcggcgagggaaccaagctgaccgtcct

aggt 3'

FIG. 4

C6ML3-9 sFv'
AMINO ACID SEQUENCE

(N-terminus to C-terminus)

-QVQLVQSGAEVKKPGESLKISCKGSGYFTSYWIAWRQMPKGLYMGL
IYPGDSDTKYSPSFQGGVTISVDKSVSTAYLQWSSLPKPSDSAVYFCARHD
VGYCSSNCAKWPYFQHWGQCTLVTVSSGGGSGGGGSG
GGGSQSVLTQPPSVSAAPGQKVTISCGSSNIGNNYVSWYQLPGTIAPK
LLIYDHTNRPAGVPDRFSGSKSGTSASLAISGRSEDEADYYCASWDYTL
SGWVFGGGTKLTVLGAAHHHHHGGGGC--

FIG. 5

C6ML3-9 sFv'
NUCLEOTIDE SEQUENCE

5'cagggtgcagctgggtgcagctcggggcagaggtgaaaaagccggggagtcctgaagatcctcgttaagggtcttgata
cagctttaccagctactggatgcctgggtgcgccagatgccgggaaagccctggagtagacatggggctcatctatcctg
gtgactctgacaccaaatacagcccgctctccaaggccaggtcaccatctcagtcgacaagtcgctcagcactgcctac
ttgcaatggagcagctcgaagccctcggacagccggtgtatttttgcgagacatgacgtgggatatattgcagtagttc
caactgcgcaaaagtggcctgaatacttccagcattggggccagggaacctggtaacctctcctcaggtggaggcgggtt
caggcggagggtggctctggcgggtggcgatcgcagtcgtgttgacgcagccgccctcagtgctctgcggccccaggacag
aaggtcaccatctcctgctctggaagcagctccaacattggggaataattatgtatcctgggtaccagcgtccccaggaaac
agcccccaactcctcatctatgatcacaccaaatcgccccgcagggtccctgaccgattctctggctccaagtctggca
cctcagcctccctcctggccatcagtggggtccgggtccgaggtgagggctgattattactgtgcctcctgggactacacccctc
tcgggctgggtgttcgggcggagggaaccaagctgacctcctcagggtgcggccgcacaccatcatcaccatcacgggtgggtgg
cggctgc 3'

FIG. 6

**C6ML3-9sFv'-L1-KDEL
AMINO ACID SEQUENCE**

(N-terminus to C-terminus)

-QVLVQSGAEVKKPGESLKISCKGSGYFTSYWIAWVRQMPKGLEYMGL
IYPGDSDTKYSPSFQGVTTISVDKSVSTAYLQWSSLKPSDAVYFCARHD
VCYCSSSNCAKWEYFQHWGQGLTVTVSSGGGSGGGGSG
GGGSQSVLTQPPSVSAAPGQKVTISCSGSSSNIGNNYVSWYQQLPGTAPK
LLIYDHTNRPAGVPDRFSGSKSGTSASLAISGRSEDEADYYCASWDYTL
SCWVFGGCTKLTVLGAHHHHHHGGGGCLESSSSGSEKDEL

FIG. 7

**C6ML3-9 sFv'-L1-KDEL
NUCLEOTIDE SEQUENCE**

5' cagggtgcagctgggtgcagctctgggggcagaggtgaaaaagccggggagtgctctgaagatctcctgtaaggggttctggata
cagctttaccagctactggatcgccctgggtgcgccagatgcccggggaaaggccctggagtagacatgggggctcatctatcctg
gtgactctgacaccaaatacagcccgctccttccaaaggccagggtcaccatctcagtcagtcgacaagtcgcgtcagcactgcctac
ttgcaatggagcagctgaagccctcggaacagcgccgtgtatttttgcggagacatgacgtgggatatatgcagtagttc
caactgcgcaaaagtgggcctgaataacttccagcatgggggcccaggcgaccctgggtcaccgtctctcctcaggtggaggcggtt
caggcgggagggtggctctggcggatcgcaagtctgtgtgacgcagccgcccctcagtgctgtcgggccccagggacag
aaggtcaccatctcctgctctggaagcagctcccaacattgggaataattatgtatcctggtaccagcagctcccaggaaac
agcccccaactcctcatctatgatcacaccaatcgggcccagggggtccctgaccgattctctggctccaagtctggca
cctcagcctccctggccatcagtggggttccggtcgcaggatgagcctgattattactgtgcctcctgggactacacccctc
tcggggtgggtgttcggcgaggagaaacaaagctgaccgctcctagtgcgggccgcacaccatcatcaccatcacgggtgggtgg
cggctgcctcagtgctctggatccgaaaaagatgaactg 3'

FIG. 8

**C6ML3-9 sFv' -L2-KDEL
AMINO ACID SEQUENCE**

(N-terminus to C-terminus)

-QVQLVQSGAEVKKPGESLKISCKGSGYFTSYWIAVVRQMPKGLEYMGL
IYPGDSDTKYSPSFQGGVTISVDKSVSTAYLQWSSLPDSDSAVYFCARHD
VGYCSSNCAKWPEYFQHWGQGLTVTVSSGGGGGGGGGG
GGGSQSVLTQPPSVSAAPGQKVTISCSGSSNIGNNYVSWYQLPGTAPK
LLIYDHTNRPAGVPDRFGSKSGTSASLAISGRSEDEADYYCASWDYTL
SGWVFGGCTKLTVLGAHHHHHHGGGGGLESSSSSGSSSGSEKDEL-

FIG. 9

**C6ML3-9sFv' -L2-KEDL
NUCLEOTIDE SEQUENCE**

5' cagggtgcagctggatgcagctcggggcagaggtagaaaaagcccgggaggtctctgaagatctcctgtaagggtcttgata
cagctttaccagctactggatgcctgggtggccagatgcccgggaaaggccctggaggtacatggggctcatctatcctg
gtgactctgacaccaaatacagcccgctcttccaaaggccaggtagccatctcagtcgacaaagtcgctcagcactgcctac
ttgcaatggagcagctgaaagccctcgacagcgccgtgtatctttgtgcgagacatgacgtgggatatgtgcagtagttc
caactgcgaaaagtggcctgaatacttccagcattggggccagggcacccctggtagccgtctcctcagggtggagcggtt
caggcggagggtggctctggcgggtggcggatcgagctctgtgttgacgcagccgccctcagtgctcgggccccaggacag
aaggtaaccatctcctgctctggaagcagctccaacatggggaataatgatgtatcctgggtaccagcagctcccaggaaac
agcccccaaaactcctcatctatgatcacaccaaatcgggcccgagggtccctgaccgattctctggctccaagtctggca
cctcagccctccctggccatcagtggggttcgggtccgaggatgaggctgattattactgtgctcctcctgggactacacccctc
tcgggctgggtgttcggcggagggaaccaaagtgaccgtcctcaggtgagggtggccgcgcacacccatcatcaccatcaggtgtgg
cggctgcctcgagctcagcagctcgggttctcctctagctcgtggatccgaaaaagatgaactg 3'

FIG. 10

C6ML3-9 sFv'-L2-H14

AMINO ACID SEQUENCE

(N-terminus to C-terminus)

-QVLVQSGAEVKKPGESLKISCKGSGYFTSYWIAWVRQMPGKLEYMGL
IYPGDSDTKYSPSFQGGVTISVDKSVSTAYLQWSSLKPSDSAVYFCARHD
VGYCSSNCAKWPEYFQHWGQGLTVTVSSGGGGGGGGSG
GGGSQSVLTQPPSVSAAPGQKVITISCGSSSNIGNNYVSWYQQLPGTAPK
LLIYDHTNRPAGVPDRFSGSKSGTSASLAISGRSEDEADYYCASWDYTL
SGWVFGGKTLTVLGAAHHHHHHGGGCGCLESSSSSSSSSS
GSKSAKTPKKAKKP-

FIG. 11

C6ML3-9 sFv'-L2-H14

NUCLEOTIDE SEQUENCE

5' caggtgcagctgggtgcagctctggggcagaggtgaaaaagcccgaggagtctctgaagatctctgttaagggttctggata
cagctttaccagctactggtcgtgggtgcccagatgccccgggaaaggcctggagtagatggggctcatctatcctg
gtgactctgacaccaataacagcccgctccttccaaagccaggctaccatctcagtcagtcagacaagtcctgcagcactgcctac
ttgcaatggagcagctctgaagccctcggacagcgcggtgtatttttggcgagacatgacgtgggatatattgcagtagttc
caactgcgcaagtggtgctgaatactccagcattggggccaggccaccctggctaccgctctcctcaggtggaggcgggtt
caggcggagggtggctctggcggatcgagctctgtgttgacgcagccgcccctcagtgctcggggcccccaggacag
aaggtcaccatctctgctctggaagcagctcccaacattgggaataattatgtatcctggtagccagcagctcccagggaac
agccccaaaactcctcatctatgatcacaccaaatcgcccccgagggtccctgaccgattctctggctcccccaagctcggca
cctcagcctccctggcccatcagtggtgtccgggtccgaggatgaggctgattattactgtgcctcctgggactacacccctc
tcgggtgggtgttcggcggagggaaccaagctgaccgtcctcaggtggcggccgcacacccatcatcacccatcacggtggtgg
cggctgcctcagctcagctccgggttcctcctcagctcgtggtatcccaagaaaaagcgcaaaaaagcccccgaaagaag
cgaagaaaccg 3'

FIG. 12

C6ML3-9sFv'-L2-nls
AMINO ACID SEQUENCE

(N-terminus to C-terminus)

-QVQLVQSGAEVKKPESLKISKGSGYSTSYWIAWVRQMPKGLEYMGL
IYPGSDITKYSPSFQGGVTISVDKSVSTAYLQWSSLKPSDAVYFCARHD
VGYCSSNCAKWPEYFQHWGQCTLVTVSSGGGGSGGGSG
GGGSQSVLTQPPSVSAAPGQKVTISCSGSSNIGNNYVSWYQQLPGTAPK
LLIYDHTNRPAQVPDRFSGSKGTSASLAISGFRSEDEADYYCASWDYTL
SGWVFGGCTKLTVLGAHHHHHHGGGGCLESSSSGSSSS
GSTPPKKRKV

FIG. 13

C6ML3-9 sFv'-L2-nls
NUCLEOTIDE SEQUENCE

5' cagggtcagctgggtcagctggggcagaggtgaaagccggggagtcctgaagatcctctgaagggttctggata
cagctttaccagctactggatcgccctgggtgcgcagatgccgggaaaggcctggagtacatggggctcatctatcctg
gtgactctgacaccaaatacagcccgctcctccaaaggccaggtcaccatctcagtcgacaaagtcctgcagcactgcctac
ttgcaatggagcagcttgaggccctcgagacagcccgctgtattttgtgagagacatgacgtgggatattgcagtagttc
caactgcgcaaaagtggcctgaatacttccagcattggggccagggcaccctggtcaccgtctcctcaggtggagggcgtt
caggcggaggtggcctctggcgggtggcggatcgagctctgtgttgacgcagcccgccctcagtgctgcggccccaggacag
aaggtcaccatctcctgctctggaaagcagctcccaacattgggaataattatgtatcctgggtaccagcagctcccaggaaac
agccccaaactcctcatctatgatcacaccaaatcgccccgaggggtccctgaccgatctctggctccaagtctggca
cctcagcctccctggccatcagtggttccgggtccgaggtgaggtgattattactgtgcctcctgggactacacctc
tcgggctgggtgttcggcggaggaaaccaagctgaccgtcctcctaggtgcggccgcacaccatcatcaccatcaggtggtagg
cggctgcctcagagctccgggttcctctagctctggatccactccggccgaaaaaagaaacgtaaagtg 3'

FIG. 14

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C6ML3-9 sFv' and its salmon protamine conjugate binds specifically to the erbB-2 positive ovarian cancer cells

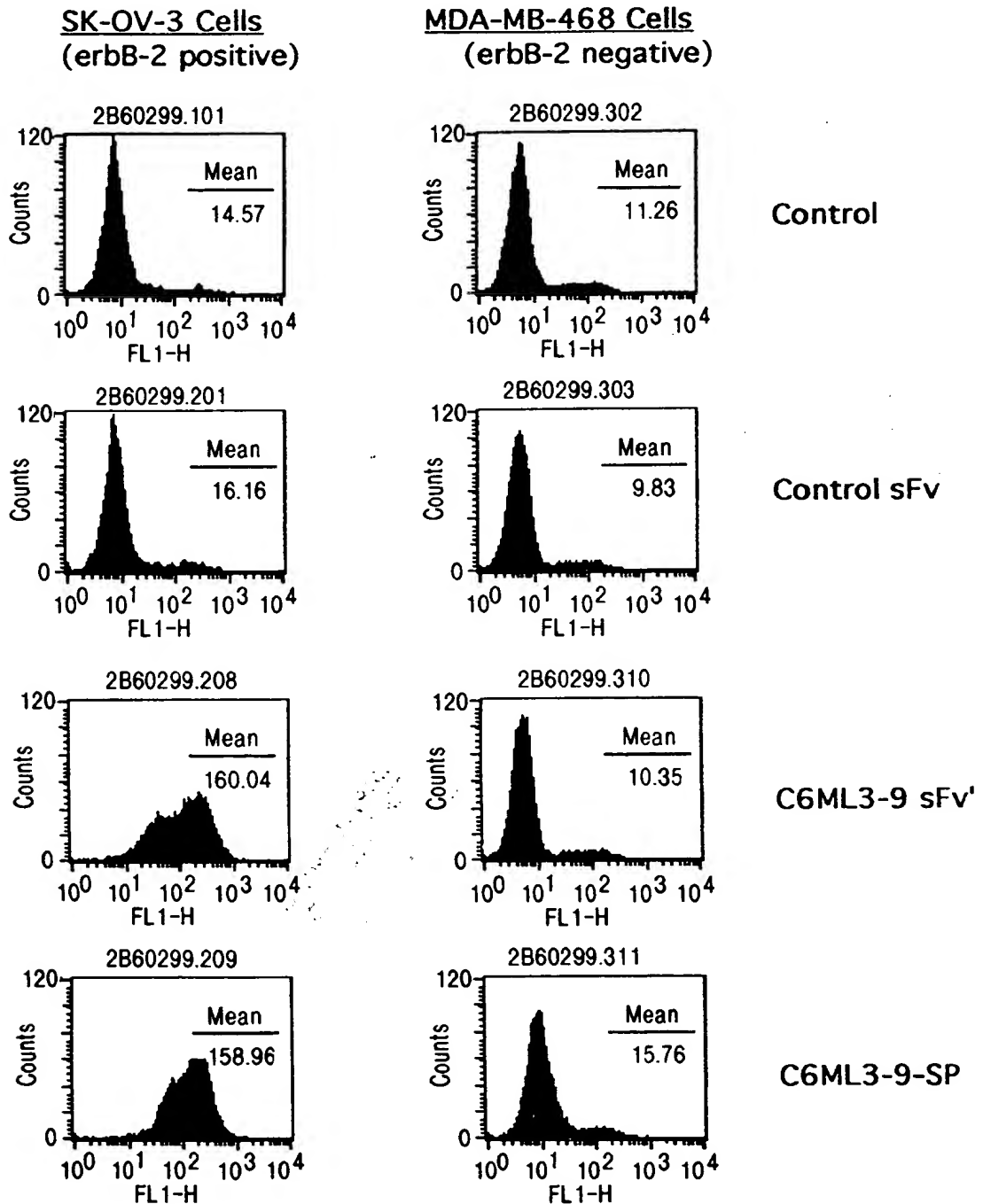


FIG. 15

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FACS Analysis of the erbB-2 Binding
Activities of Bacterially Expressed C6ML3-9 sFv'
and its Derivatives

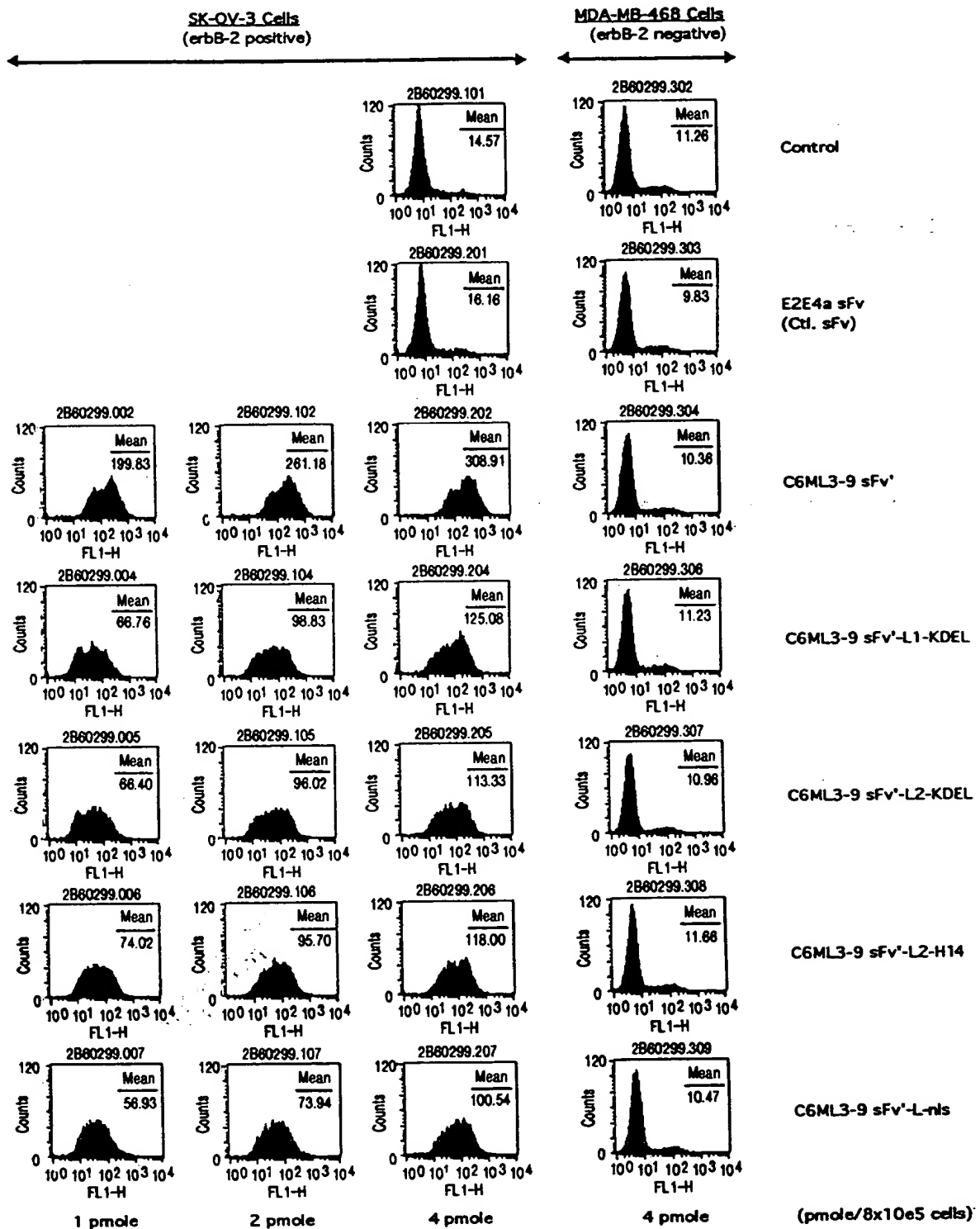
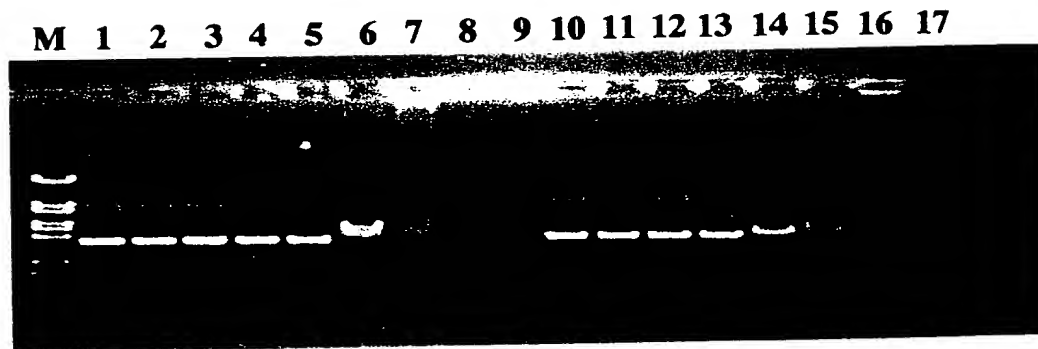


FIG. 16

Gel Shift Analysis of the C6.5-SP-DNA and C6ML3-9-SP-DNA Complex

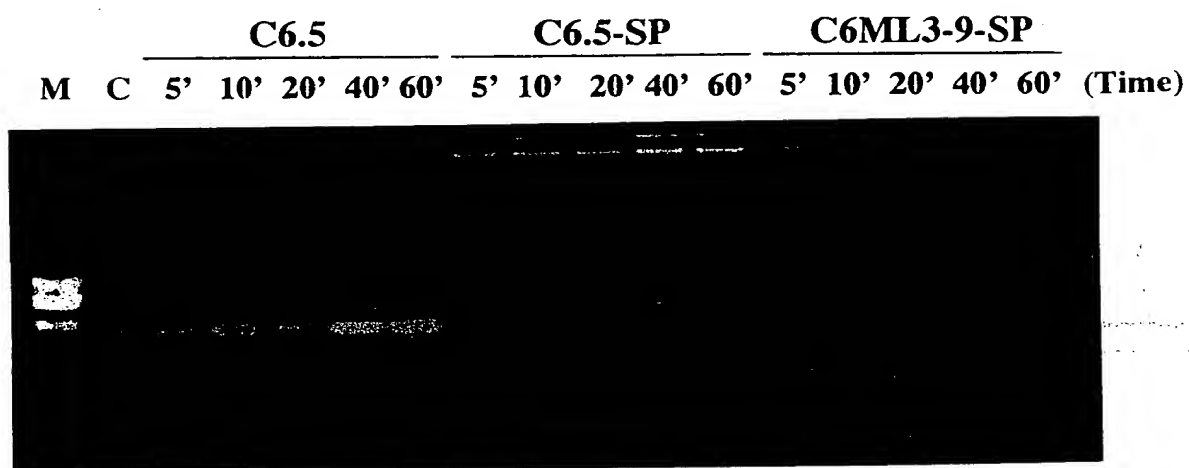


- M. DNA marker - λ DNA BstEII digest
1. 200 ng pGL3 DNA
 2. 200 ng pGL3 DNA + 1.45 pmol C6.5
 3. 200 ng pGL3 DNA + 2.90 pmol C6.5
 4. 200 ng pGL3 DNA + 5.80 pmol C6.5
 5. 200 ng pGL3 DNA + 11.6 pmol C6.5
 6. 200 ng pGL3 DNA + 1.45 pmol C6.5-SP
 7. 200 ng pGL3 DNA + 2.90 pmol C6.5-SP
 8. 200 ng pGL3 DNA + 5.80 pmol C6.5-SP
 9. 200 ng pGL3 DNA + 11.6 pmol C6.5-SP
 10. 200 ng pGL3 DNA + 1.45 pmol C6ML3-9
 11. 200 ng pGL3 DNA + 2.90 pmol C6ML3-9
 12. 200 ng pGL3 DNA + 5.80 pmol C6ML3-9
 13. 200 ng pGL3 DNA + 11.6 pmol C6ML3-9
 14. 200 ng pGL3 DNA + 1.45 pmol C6ML3-9-SP
 15. 200 ng pGL3 DNA + 2.90 pmol C6ML3-9-SP
 16. 200 ng pGL3 DNA + 5.80 pmol C6ML3-9-SP
 17. 200 ng pGL3 DNA + 11.6 pmol C6ML3-9-SP

*0.8% agarose gel in 1xTAE, 150v, RT, ~1hr, EtBr staining overnight

FIG. 17

Kinetic Study of the C6.5-SP-DNA and C6ML3-9-SP-DNA Complex Formation



M. DNA marker - λ DNA BstEII digest

C. 200 ng pGL3 DNA alone

* The rest of the lanes - 200 ng pGL3 DNA incubated with 5.8 pmol proteins as indicated above each line, on ice, for different period of time. Electrophoresis condition same as Figure 17.

FIG. 18

**The C6ML3-9-SP conjugate protein mediates
specific luciferase gene delivery to erbB-2 positive cancer cells**

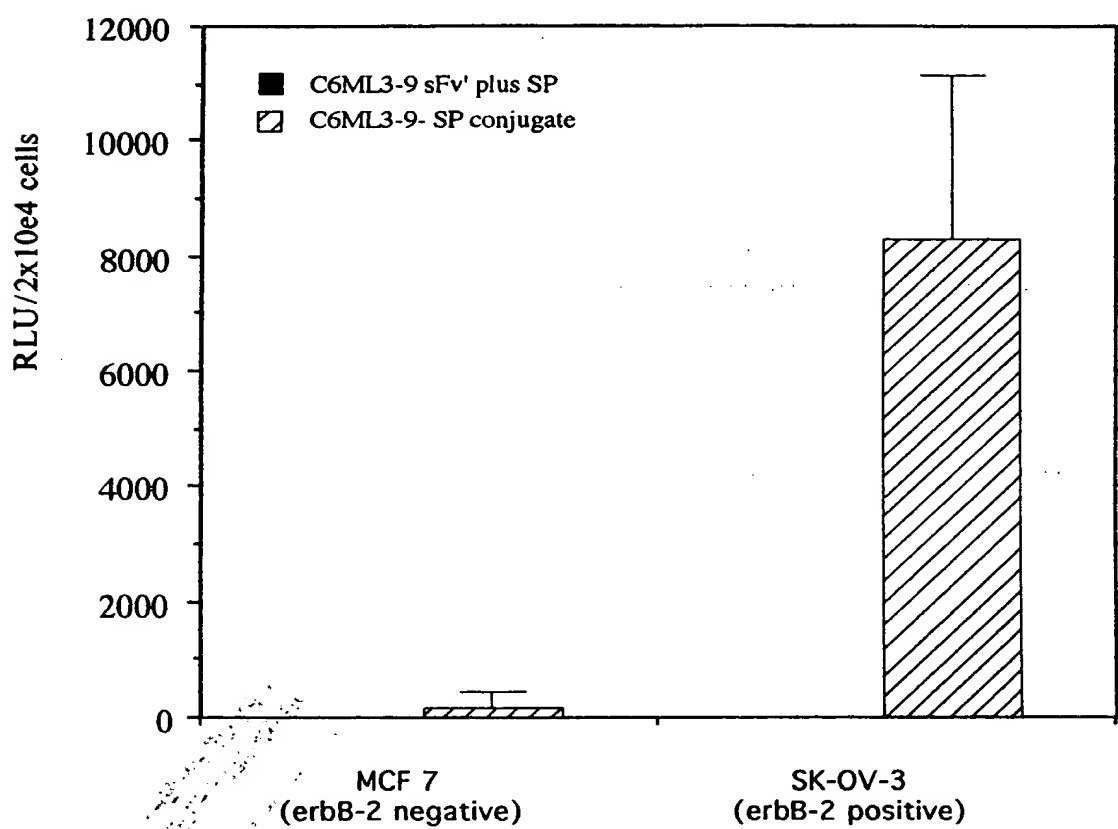
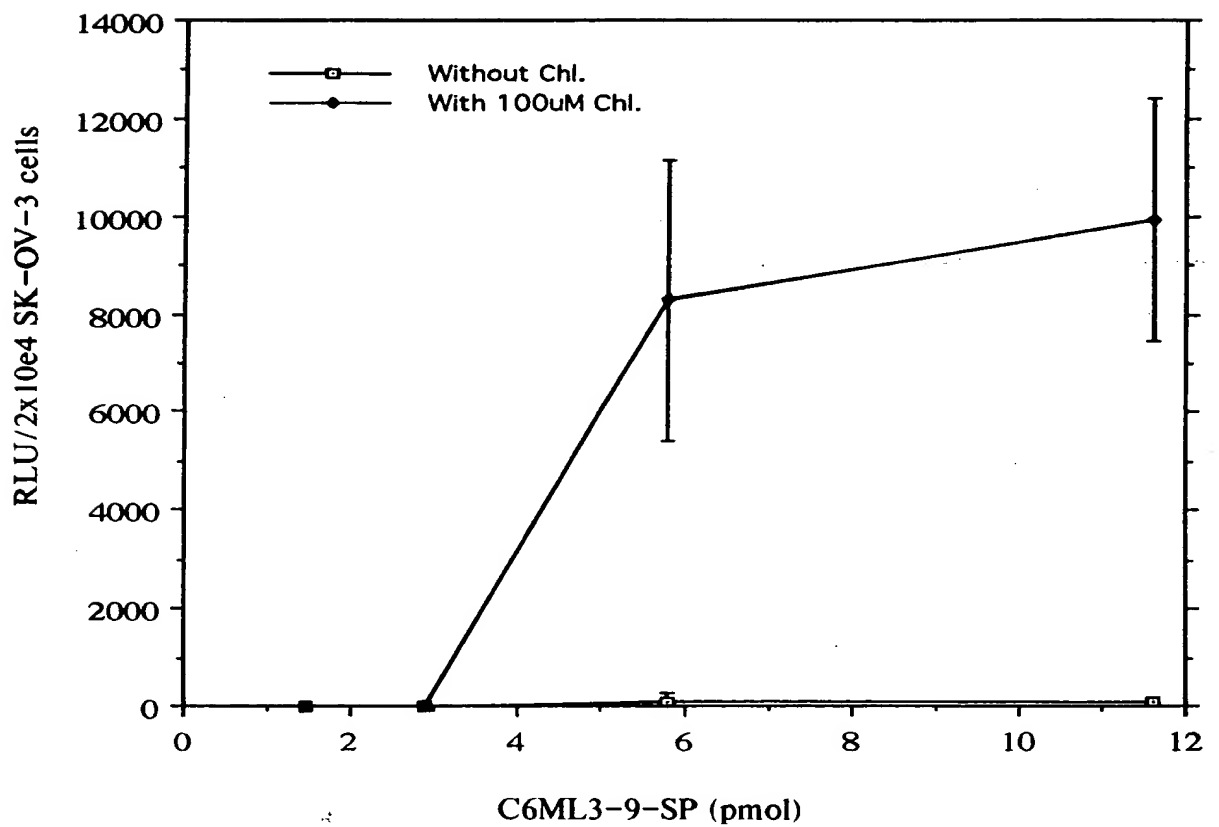


FIG. 19

Chloroquine-dependent C6ML3-9-SP-mediated Gene Delivery

**FIG. 20**

Fluorescent microscopy of C6.5-SP and C6ML3-9
-SP-mediated gene transfer of pGeneGrip Rhodamine/GFP
plasmids with SK-OV-3 and MCF-7

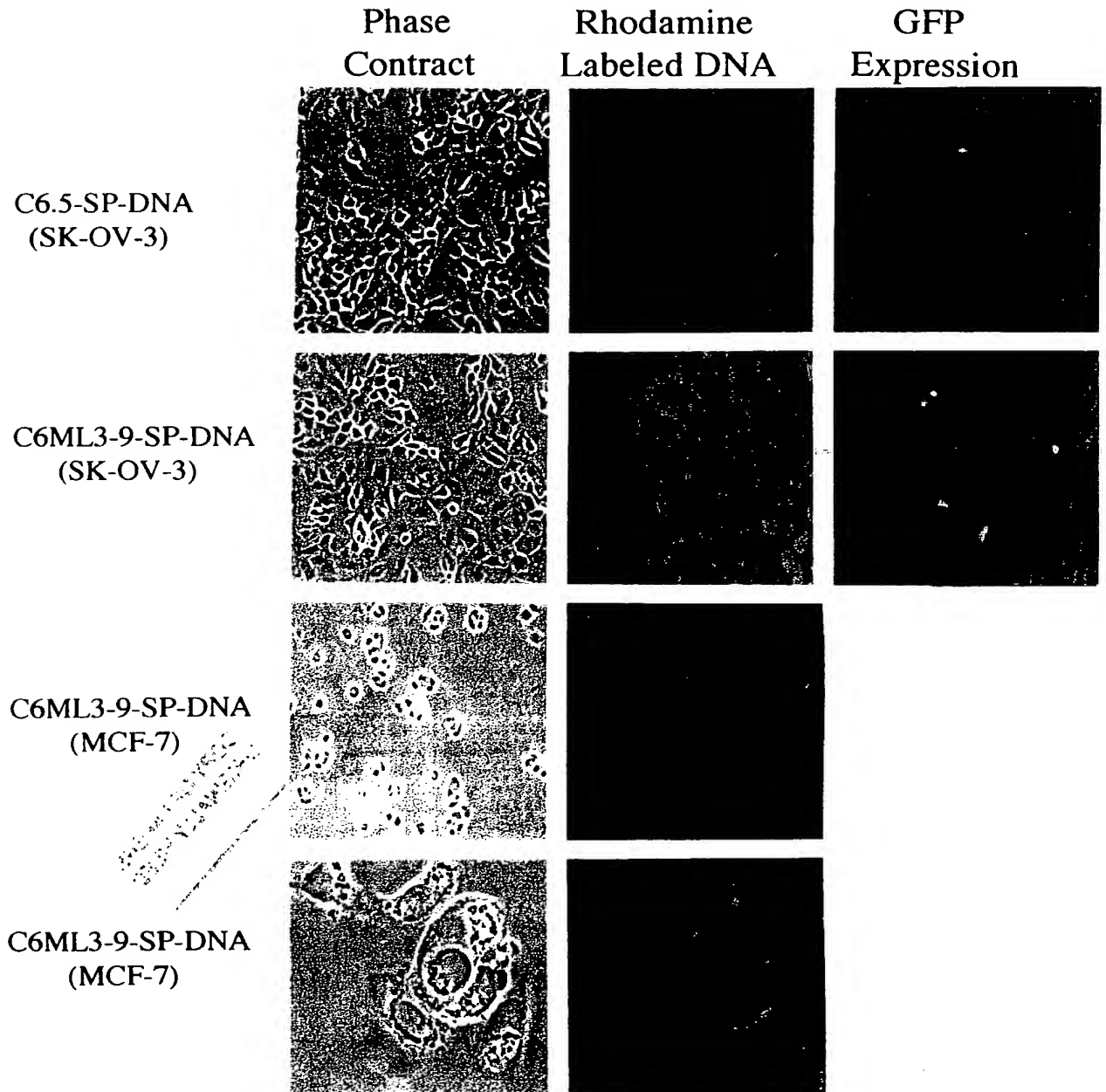


FIG. 21

THE EFFECT OF
CHLOROQUINE ON 3T3-HER2 TRANSFECTION
MEDIATED BY C6ML3-9sFv'-SALMON PROTAMINE

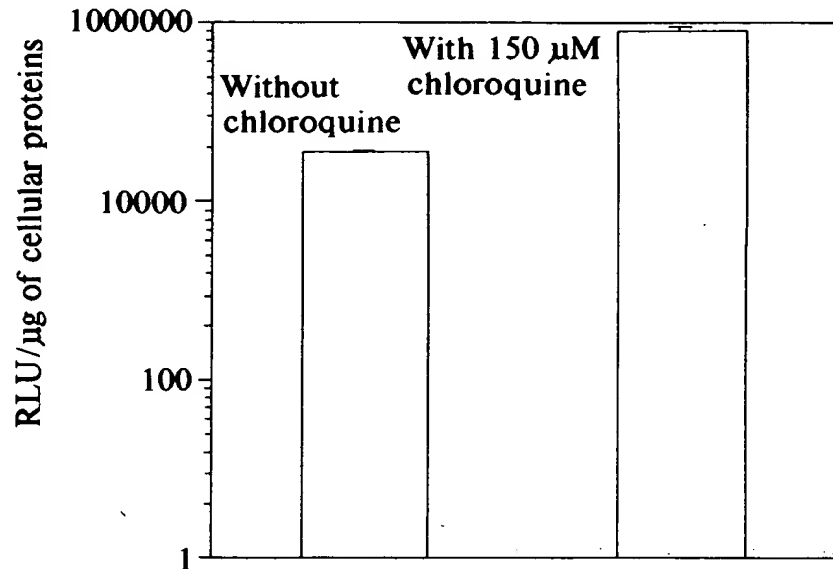


FIG. 22

THE EFFECT OF CHLOROQUINE ON 3T3-HER2
TRANSFECTION MEDIATED BY C6ML3-9sFv'#2-P1

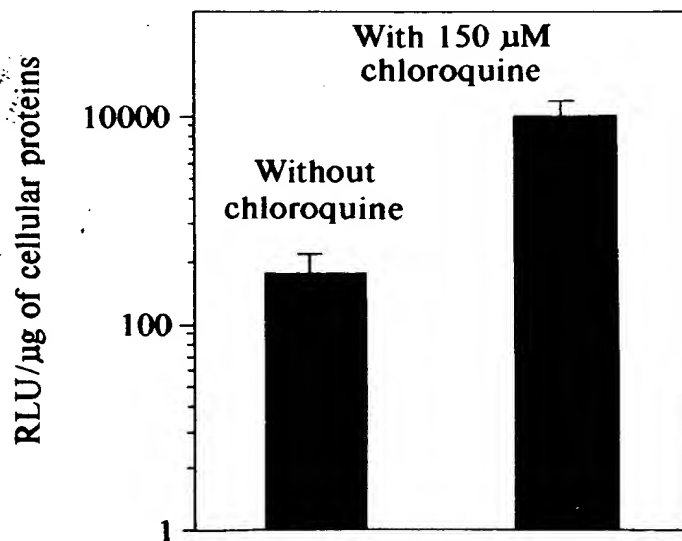


FIG. 23

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THE EFFECT OF CHLOROQUINE ON 3T3-HER2 TRANSFECTION MEDIATED BY C6ML3-9sFv'#2-H1

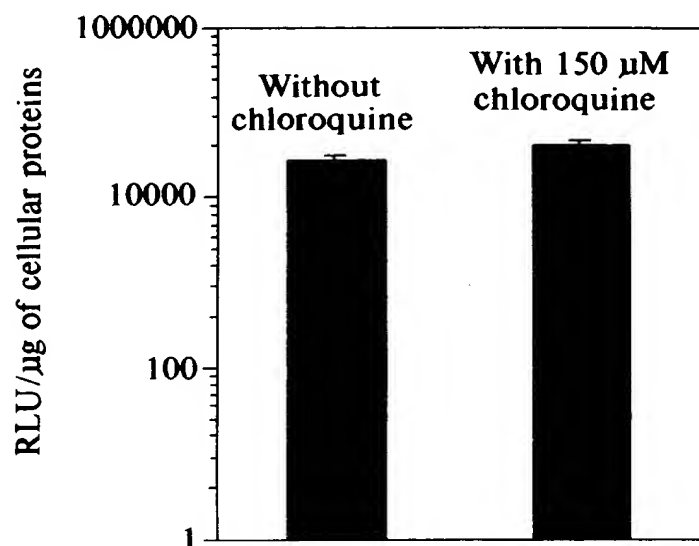


FIG. 24

THE EFFECT OF C6ML3-9sFv'-H1-pBks ON 3T3-HER2 TRANSFECTION MEDIATED BY C6ML3-9sFv'-H1

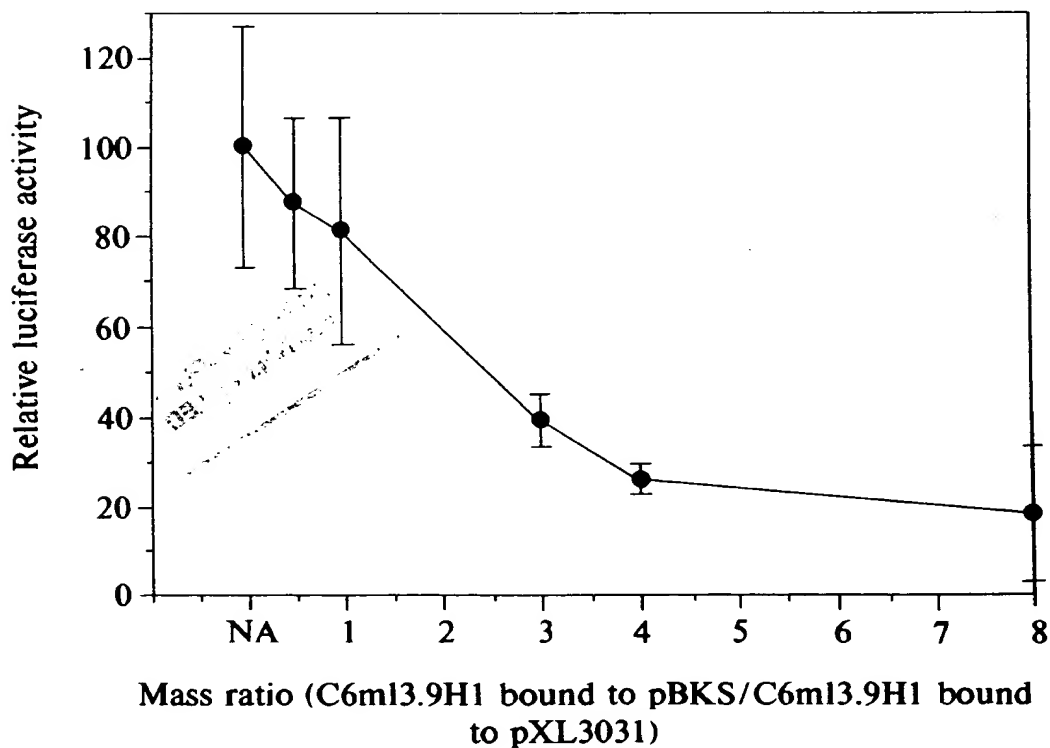


FIG. 25

THE EFFECT OF THE DNA TO C6ML3-9sFv'-H1
RATIO ON 3T3-HER2 TRANSFECTION EFFICIENCY

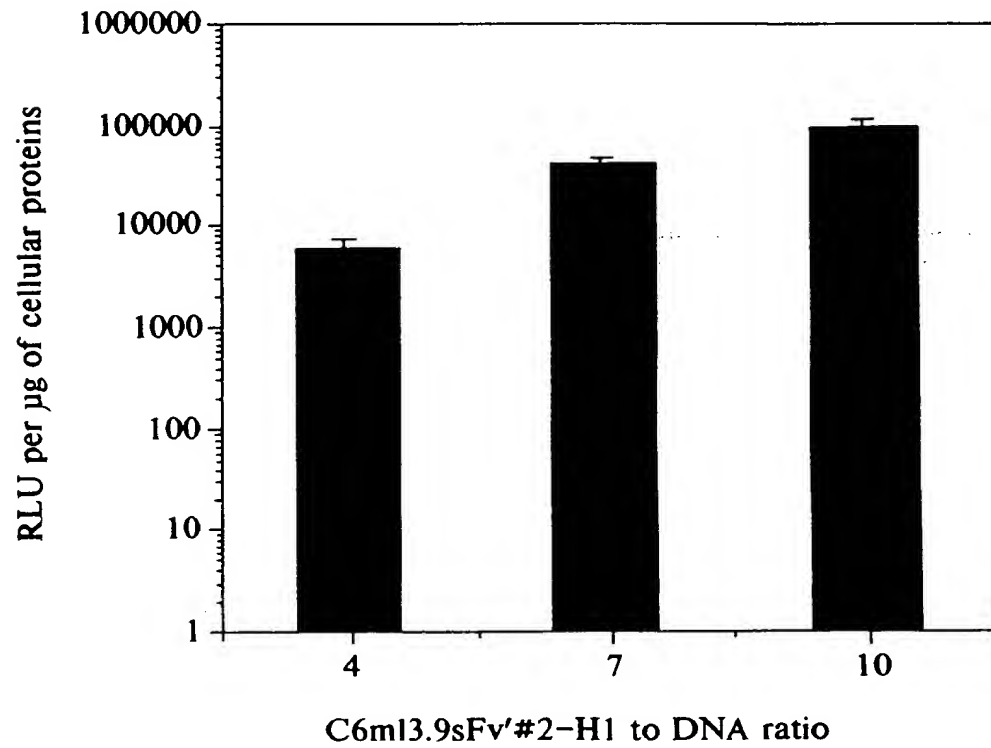


FIG. 26